Saliva produced by stimulating the chorda tympani, or by injecting pilocarpin, after a small dose of atropin has been given, contains a low percentage of organic substance and of salts.

We, like Werther, find that sub-lingual saliva has a considerably higher percentage of salts than sub-maxillary saliva.

If lithium citrate, potassium iodide, potassium ferrocyanide, and pilocarpin are injected into the blood, lithium can be detected in the first drops of saliva secreted, potassium iodide after the first six drops; potassium ferrocyanide cannot be detected at any stage of secretion.

The general result of these experiments is to show that the secretion of water, of salts, and of organic substance are differently affected by different conditions, and that the percentage composition of saliva is determined by the strength of the stimulus, by the character of the blood, and by the amount of blood supplied to the gland.

All or nearly all the arguments which have been adduced to prove that the secretion of organic substance is governed by special nerve-fibres, have their counterparts with regard to the secretion of salts, so that we might imagine at least three kinds of secretory fibres to be present. The experiments, on the whole, indicate that this complicated arrangement does not exist, but that the stimulation of a single kind of nerve-fibre produces varying effects according to the varying conditions of the gland cells.

IV. "Observations upon the Electromotive Changes in the Mammalian Spinal Cord following Electrical Excitation of the Cortex Cerebri. Preliminary Notice." By Francis Gotch, Hon. M.A. Oxon, B.A., B.Sc. Lond., and Victor Horsley, B.S., F.R.S., Professor of Pathology, University College, London. (From the Physiological Laboratory of the University of Oxford.) Received August 27, 1888.

[Plate 1.]

Hitherto pathologists have attempted the analysis of the epileptic convulsion by the graphic method, that is, by recording the spasmodic contractions of the muscles involved. Recent investigations of this kind have shown that the excitation of the cortex cerebri, whether by electrical or chemical means, or by the presence of certain pathological states, neoplasms, inflammation, &c., is invariably followed in the higher mammals by a definite and characteristic sequence of movements in the muscles. It is, however, obvious that such investigations have up to the present succeeded in determining the characters of the neural disturbance only when this has reached the peripheral

terminations of the efferent nerves. Now since the excitatory processes originating in the cortex are conducted by the efferent channels in the spinal cord, presumably the pyramidal tracts, the problem of their relationship to the centres of the bulbo-spinal system cannot be determined by experiments which record the mechanical changes in the muscles. In order to ascertain what share respectively the centres in the cortex and those in the spinal cord have in the production of the characteristic epileptic sequence, the action of the latter must be eliminated. This can be done by investigating the nature of the excitatory processes in the cord when the efferent channels in the dorsal region for the lower limbs are made the subject for observation.

For this purpose we determined to obtain, if possible, evidence as to the nature of the excitatory processes of the epileptic convulsion in the spinal cord, as shown by "tapping" the cord and noting the electromotive changes which, as is well known, accompany functional activity in nerves. The results we have already obtained are so harmonious and demonstrative, that we venture to make this preliminary communication, reserving full details for a subsequent account.

Part I. *The Electromotive Change following a Single Excitation of the Mammalian Nerve.*

Our first experiments were made for the purpose of ascertaining to what extent we could detect an electromotive change following a single excitation of a mammalian nerve. Since the discovery by du Bois-Reymond of the fact that the excitatory process in nerve is accompanied by an electromotive change, the characters and time relations of this change have been investigated by various observers, notably by Bernstein, Hermann, Hering, and Head. The general result of their observations is to show that the change following a single stimulus is of very short duration, so short that the galvanometer gives little evidence of its presence, and the observers referred to were compelled to adopt the device first employed by Bernstein, which involves repeated excitation and consequent summation of effect, a method well known to physiologists as that of the repeating differential rheotome. For our purpose it was essential to obtain evidence of the effect following one stimulus only, and this we were fortunately able to do by using a sensitive Lippmann's capillary electrometer of quick reaction, made by Mr. G. F. Burch, and belonging to Dr. Burdon Sanderson, who kindly placed it at our disposal. This instrument, when the capillary was magnified 400 times by the observing microscope, gave a perceptible response when connected through a resistance of 10,000 ohms for one-thousandth of a second with an electromotive difference of only 0·003 D. The amount of movement of the mercury was estimated by the divisions of a micrometer eyepiece, one

division of which indicated an actual movement of $\frac{1}{400}$ of a millimetre. After we had found that the electrometer, when connected with the transverse and longitudinal surfaces of the sciatic nerve of the toad, showed a response of one division following the application of a single stimulus, whether electrical or mechanical, we proceeded to the examination of the sciatic nerve in the rabbit, cat, and monkey. For these experiments the animal was in every case kept under the influence of ether, which was maintained throughout the whole experiment, and the animal was killed before recovery. The sciatic nerve seemed for many reasons the most suitable of the mammalian nerves. It can be quickly prepared for 7 or 8 cm. in length; its nutrition is well preserved, since the *arteria comes nervi ischiadici* can be left uninjured, and its diameter lessens the dangers of drying.

The nerve, having been rapidly prepared and bathed in warm saline solution, 0·6 per cent., was ligatured low down in the thigh, the ligature including the popliteal trunks. It was then divided on the peripheral side of the knot, and raised in air so as to be at right angles to the limb. One kaolin pad of a non-polarisable electrode was applied to the cut end, and another to the longitudinal surface at a distance of 1·5 cm. A pair of sheathed exciting platinum electrodes 2 mm. apart, was then applied to the trunk of the nerve 6 cm. centrally from the nearest leading-off electrode, *i.e.*, opposite the sciatic notch. The exciting stimulus was obtained by the break of the current of a single Callaud cell supplying the primary coil of a du Bois-Reymond inductorium graduated by Kronecker. The break shock produced in the secondary coil by this means was so feeble as to be barely perceptible on the tip of the tongue when the secondary coil completely covered the primary. The break was effected by the spring rheotome, which opened a fixed key at a definite point in its course. The electrometer was connected with the non-polarisable electrodes by a circuit which included the usual compensator. By means of a switch the electrometer could be cut out, and the circuit made to include a high resistance galvanometer, which also revealed the single variation. The two instruments could be thus readily compared. The excursion of the mercury of the electrometer was ascertained both by direct observation in terms of the divisions of the micrometer eyepiece, and by photographing the projected capillary upon a moving sensitive plate; in the latter case the capillary was magnified 100 times. The results of our observations are briefly as follows:—

The mammalian nerve showed a well-marked difference or demarcation current, that is to say, the electrode upon the longitudinal surface was notably positive to that on the cut end. The movement of the mercury corresponding to this difference amounted in some cases to 60 divisions of the micrometer, and is shown in fig. 1 pro-

jected upon the plate. Its E.M.F. was from about 0·01 to 0·015 D. The passage of the single break induction shock through the platinum electrodes in either direction was followed by a small quick movement of the mercury, which was invariably in the opposite direction to that produced by the demarcation current. Its amount varied in different animals from 1 to 2·5 divisions of the micrometer eyepiece, and it is shown as photographed in fig. 1 and fig. 2. After severing the nerve from the bulbo-spinal system above the exciting electrodes, the same effect was obtained; its character, as shown by the movement of the mercury was, however, different, being as we believe much shorter in duration and less in amount. But our experiments not being directed to the elucidation of this point, we will not speak positively with regard to it. After a time, varying in different cases from twenty minutes to three-quarters of an hour, the effect was no longer visible. This movement of the mercury may be conceivably due to the three following factors, working singly or in co-operation:—

(A.) Escape of the exciting induction current (uni-polar).

(B.) Electrotonic change.

(C.) The true excitatory variation of the nerve.

(A.) That it was not due to any escape of the induction current is shown by the following facts:—

(1.) The variation was produced by the very weak induction currents, such as those obtained when the Helmholtz wire is used, and its character did not vary with increasing strength of the current.

(2.) It was no longer perceptible when the nerve was ligatured between the exciting and leading-off electrodes.

(3.) As the nerve gradually died the effect became less, and was no longer perceptible when the nerve was severed from the animal and left for three-quarters of an hour. Moreover, when the nerve was indifferently prepared the variation was absent, or else very small and transient.

(4.) The effect remained visible when the electrometer was short circuited for $\frac{2}{1000}$ second after the break of the exciting key.

(B.) That it was not due to electrotonic change is shown by the following additional facts:—

(1.) The direction of the effect was always the same, that is, opposed to that of the demarcation current whatever the direction of the exciting current.

(2.) When the exciting electrodes were shifted to within a centimetre of the proximal leading-off electrode, an effect was produced, the direction of which was dependent upon that of the exciting current (fig. 3). This effect differed from that of the true variation in other particulars, viz., its amount was dependent upon that of the

exciting current, it could be obtained after ligature of the nerve, and when thus obtained its character, as shown by the movement of the electrometer, was unlike that of the excitatory variation, both to the eye and in the photograph (compare figs. 1, 2, 3, Plate 1).

(3.) An excursion similar to that we are considering could be produced by mechanical excitation.

There is thus no doubt that the movement we obtained and photographed was due to the electromotive change which accompanies the propagation of an excitatory state along the mammalian nerve when this state is evoked by the application of a single stimulus.

Having thus assured ourselves of the accuracy of the method, we now proceeded to ascertain whether the instrument would reveal the existence of similar electromotive changes if it was connected with the nerve or with the spinal cord, and an epileptic convulsion produced by excitation of the cortex cerebri.

PART II. *Excitation of the Cortex Cerebri.*

A. *Mixed Spinal Nerve connected with the Electrometer.*—In two cases we have connected in the manner described in Part I the sciatic nerve with the electrometer, and have then exposed by a small trephine opening the so-called motor cortical centre for the lower limb. This we then excited by a very weak but adequate faradic current. So far, however, we have not been able to detect any movement in the mercury, although the muscles of the investigated limb supplied by the anterior crural nerve were thrown into a state of active convulsion. It is probable that the character of the neural disturbances in the mixed nerve may be best studied by investigations which we shall shortly undertake upon the electromotive changes in the muscles.

B. *The Spinal Cord connected with the Electrometer.*—The experiments, the results of which are now to be briefly detailed, were made in the following manner:—

The spinal cord of the etherised animal (cat and monkey) was exposed in the lower dorsal region for about 4 cm., and as low down as the upper end of the lumbar enlargement. Great care was taken by bathing with warm saline to guard as much as possible against the dangers of error due to cooling and drying. The dura mater having been split longitudinally, a strong thread was passed round the spinal cord at the lower limit of the part exposed. It was tied firmly and the cord divided below the knot. By successive division of the two or three roots exposed in the intervertebral foramina, the cord was easily raised from the neural canal and suspended in the air without any great interference with the circulation in the longitudinal vessels.

One of the non-polarisable electrodes was then brought into contact with the cut end of the cord and the knotted ligature, while the other was connected with the longitudinal surface of the cord 2 cm. from the cut end by means of soft thread cables soaked in saline solution and tied loosely round the cord. In one experiment the connexion was with one lateral column only. Mass movements of the electrodes upon the spinal cord were suitably guarded against, though it was found that the cord might be shaken without producing any effect in the electrometer.

On connecting these electrodes with the electrometer a considerable electromotive difference was found to exist between the contacts, the excursion of the mercury being so great, *i.e.*, beyond the field of the microscope, that its amount could not be estimated in terms of the micrometer eyepiece. The cut surface was always negative to the longitudinal surface, and the amount of the difference as estimated by the compensation method was about 0·02 D. It appeared to be highest when the section passed through the dorsal region without involving the lumbar enlargement. A difference between the surfaces of the cord has been previously observed by du Bois-Reymond.

The cortex cerebri was now exposed and the exciting circuit prepared. The inductorium previously employed was again used with one Daniell cell in connexion with the interrupter of primary coil and the Helmholtz side wire. The exciting electrodes had platinum points 2 mm. apart.

The demarcation current having been compensated, and the electrometer placed in connexion with the non-polarisable electrodes, the motor area for the lower limb was excited. The results of the observations made upon four monkeys and several cats may be summed up as follows:—

(1.) The application of the exciting electrodes to the cortex was without exception only followed by a movement in the electrometer when the area of representation of the lower limb was touched, and this even when owing to prolonged excitation of the arm area the upper limb was in violent epileptic convulsion. We found that when the exciting electrodes were moved over the surface of the brain the observer at the electrometer only gave notice of a movement in the instrument when the person exciting had crossed the margin of representation of the limbs. This shows that electromotive changes in the cord sufficient to affect our instrument occurred only when the motor area of the lower limb was excited. All error due to escape is thus set on one side, while at the same time this remarkable fact confirms the localisation of function.

(2.) The excitation of the motor area for the lower limb was accompanied and followed by characteristic movements of the mercury (figs. 4 and 5). The excitation by means of the interrupted

current usually lasted for two seconds, that is about 200 equal and alternately directed induction currents passed through the excited tissue. During this period the mercury showed an excursion opposed in direction to that of the difference between the longitudinal surface and cut end of the cord. This excursion persisted as long as the excitation lasted, and ceased when this was left off. Then after an interval of from one to three seconds there ensued a rhythmical succession of excursions each opposed in direction to the resting difference, some apparently single and others multiple. These lasted from twenty to thirty seconds and suddenly ceased.

The excursions varied in amount from one to about four divisions of the micrometer eyepiece, and their rate of occurrence was too rapid to be correctly estimated by the eye. We therefore obtained photographs of this rhythmical effect, and of these we append two (see figs. 4 and 5). The first of these (fig. 4) shows the electromotive change occurring in the spinal cord during a complete convulsion, in which may be distinguished the first persistent stage parallel to the tonic stage of the muscular epileptic convulsion and the second rhythmical series parallel to the clonic stage.

They are both shown upon the plate, which in this instance took about twelve seconds in travelling past the image of the capillary.

The second photograph (fig. 5), taken on a quickly travelling plate, shows the rhythmical stage only. The rate of the rhythm is seen to vary, and the individual variations to become more pronounced as the rhythm slows, that is, towards the end of the fit.

We have repeated this observation thirty or forty times, and feel ourselves justified in concluding that we have obtained evidence that during a cortical epileptiform discharge the electromotive changes in the spinal cord are exactly parallel as regards the character of their sequence to the convulsions of the muscles as recorded by the graphic method. It remains to be stated that after removal of the cortex we have obtained an effect in the electrometer when the corona radiata was stimulated. This effect was only present during the period of excitation, no rhythmical after-effect ever being observed. Its character was prolonged, and resembled the persistent stage referred to above (see fig. 6).

In conclusion, we consider that since by the method we have adopted the influence of the lumbar bulbo-spinal centres is excluded, the existence of the epileptic rhythm in the dorsal regions of the spinal cord points to its being almost entirely of cortical origin.

Fig. 1.

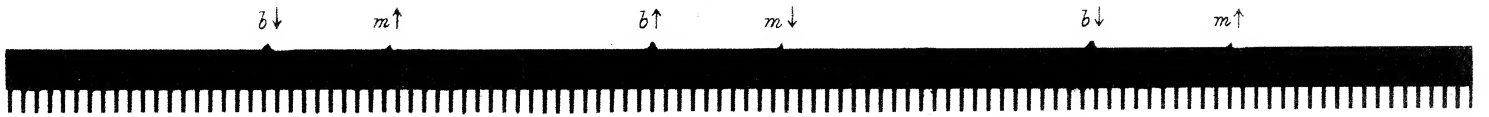

Fig. 2.

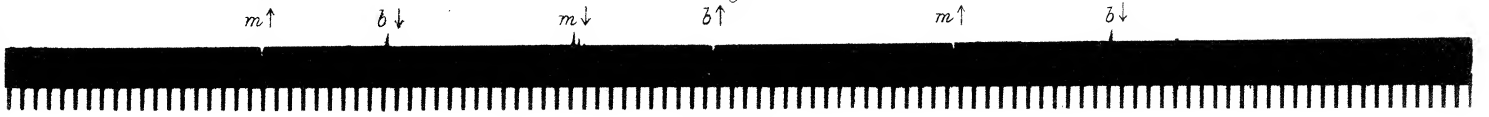

Fig. 3.

Fig. 4.

Fig. 5.

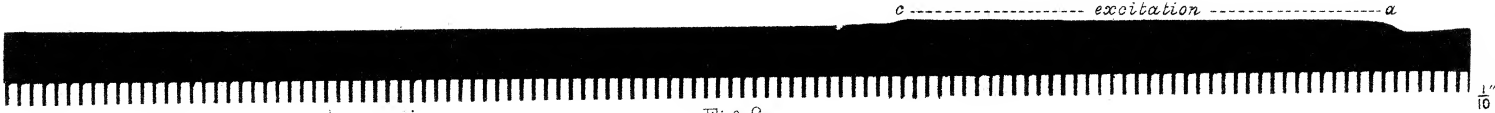

Fig. 6

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EXPLANATION OF PLATE 1.

The six figures in the plate are facsimile drawings of photographs. The negatives were obtained by projecting the image of the capillary electrometer upon a narrow slit, behind which an extra rapid photographic plate travelled. The direction of movement was such that the right hand side of the prints corresponds to the moment when the plate reached the slit: the figures are thus to be read from right to left. In order to save room, only the essential part of the photographs—that showing the position of the meniscus of the mercury in the photograph—is shown. The lower darkly toned part of each figure corresponds to the lighter part of the negative, and indicates the part of the slit shaded by the mercury of the electrometer; an excursion of the mercury is thus indicated by an elevation or depression of the upper edge of the dark band. The regular series of dark and light bars on the edge of the figures were made by a vibrating shutter, each entire vibration of which occupied one-tenth of a second.

FIG. 1.—Photograph showing two prominences, *m* and *b*, due to two excursions of the mercury when first a make and then a break induction shock was led through the mammalian nerve, the cut end and surface of which were in connexion with the electrometer 6 cm. from the point of excitation. The arrows indicate the direction of the exciting induction current through the nerve, and the effect is seen to be independent of this direction. At the point marked * the electrometer was short circuited, and the movement of the mercury due to the cessation of the demarcation current effect is thus shown. The excursions at *m* and *b* are seen to be opposed in direction to that produced by the demarcation current.

FIG. 2.—Photograph showing the excitatory variation effect in nerve. In this case the nerve of the monkey was severed from the body, connected as in fig. 1 with the electrometer, and excited six times by means of induction shocks of different character and direction. The excitation occurred at make *m* and break *b*, and the direction of the induction shock—whether ↑, ascending, or ↓, descending—is indicated. The effect is seen to be always in the same direction, being opposed to that of the demarcation current, and such that the electrode on the longitudinal surface becomes negative to that on the cut section. The rate of movement of plate was the same as in fig. 1.

FIG. 3.—Photograph illustrating the effect produced in the electrometer when there is a slight escape from the exciting electrodes into the electrometer electrodes. The effect was produced by using a severed nerve, which no longer gave any obvious excitatory response to electrical excitation. The exciting electrodes were placed upon such a nerve at a very short distance (1·5 cm.) from the nearest leading off electrode, viz., that upon the longitudinal surface. The direction of the effect is seen to depend upon the direction of the induction shock as produced by make *m* and break *b* of the primary circuit of the induction apparatus. The character of the excursion is markedly different to that shown in figs. 1 and 2, being much more abrupt. The rate of movement of plate was the same as in fig. 1.

FIG. 4.—Photograph showing the effect produced in the electrometer when this is connected by one pole with the longitudinal, and by the other with the sectional, surface of the spinal cord of the monkey, and the *cortex cerebri* then excited over the motor area for the lower limbs by means of the faradic current. The excitation commenced at *a* and ceased at *c*. It is seen to be accompanied by an upward movement of the mercury, shown by an alteration in the position of the dark band, which reaches a slightly

higher level and remains at this level during the period of excitation, and then returns. The direction of the movement indicates that the longitudinal surface has become negative to the cross-section. This corresponds to the persistent (tonic) muscular effect which is characteristic of the first stage of an epileptic fit. Proceeding from right to left, the cessation of the excitation is seen to be followed by a rhythmical series of excursions, which at first follow one another in rapid succession, but are small in extent, and which subsequently occur at longer intervals, but are much more pronounced in character, until at *d* they suddenly cease. This corresponds to the clonic stage of the epileptic convulsion.

Fig. 5.—The photograph shows the rhythmical (clonic) effect only. The recording surface was made to travel more rapidly past the slit, a marked rhythmical change having been first evoked by excitation of the cortex. The plate was not allowed to commence its passage past the slit until six seconds after the excitation had ceased. The rhythm is thus seen to great advantage. As before, the upward movement of the mercury, as indicated by the elevations of the more darkly toned parts, are due to electromotive changes in the cord such that the longitudinal surface of the cord becomes negative to the transverse section.

Fig. 6.—Photograph showing the effect obtained when, with the spinal cord connected as in the preceding with the electrometer, the *cortex cerebri* is removed and the *corona radiata* excited by faradisation. The excitation commenced at *a* and ceased at *c*. It is accompanied by an upward persistent movement of the mercury, shown in the photograph as an alteration of level, and corresponding in character to the (tonic) effect produced during the excitation of the cortex. On the cessation of the stimulus the effect subsides and is *not* followed by any rhythmical effect.

Presents, November 15, 1888.

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Fig 1

Fig 2

Fig 3

Fig 4

Fig 5

Fig. 6.